REMARKS

This application pertains to novel solid lipid particles of bioactive agents and methods for the manufacture and use thereof.

Claims 1-40, 42, 44 and 45 are pending.

Claims 41 and 43 have been canceled in response to the previous office action.

Claims 1-15 and 37-39 are withdrawn from consideration, while Applicant still desires to traverse the restriction requirement.

Reconsideration and withdrawal of the restriction requirement is respectfully requested as for the reasons already stated in the response to the restriction requirement.

In case the Examiner still does not find it possible to withdraw the restriction requirement, it is respectfully requested that the non-elected subject matter be rejoined with the elected subject matter upon allowance of the elected subject matter.

Contrary to the foregoing the Examiner states that Claims 37-39 have been canceled as well, which in fact is not the case. These Claims are only withdrawn from consideration. Appropriate correction is kindly requested.

Amendments to Claims

Claims 16, 26 and 40 have been amended to recite that step a) of the method is conducted at “room temperature”, which is supported by the description of the application in para. [0129].

No new matter is introduced.

Rejections under 35 USC § 103

Claims 16-36, 40, 42 and 44-45 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Westesen et al. (US 5,885,486) in view of Timothy et al. (Biotechnol. Prog. 2000, 16, 402-407).

With regard to the Westesen et al. reference, the examiner states that the Westesen et al. reference pertains to the area of administrative forms and delivery systems for drugs, vaccines and other biologically active agents, as well as to processes for the preparation of suspensions of colloidal solid lipid particles (SLPs) (…) and of suspensions of micron and submicron particles of bioactive agents (PBAs) (Abstract).

Turning to Applicant's Claims 16, 26 and 40 in comparison to the Westesen et al. reference with regard to the SLP production process as stipulated in col. 11, lines 6-57, the Examiner contends that the Westesen et al. reference discloses all limitations of Applicant's Claim 16, except the addition of compressible fluid in the supercritical state under pressure to the suspension, as stipulated in part b) of Applicant's Claim 16, 26 and 40.

In response to the arguments not held persuasive by the Examiner, that the sequence of steps is not met by the Westesen et al. reference, the Examiner argues, that it would be obvious to one of ordinary skill in the art to either melt the drug before or after it was suspended in dispersant.

Within this argumentation the Examiner turns step (4) (col. 11, lines 21-24) of the Westesen et al. reference, to prove that Westesen et al. discloses that "the drugs or bioactive substances may be melted or may be dissolved, solubilized or dispersed in the lipid melt, see col. 11, step (4). (and that) The melted lipid compounds are emulsified in the dispersion medium, see step (5) on column 11."

Aside from the fact that "step (4)" does not disclose the fact mentioned by the Examiner, Applicant's believe that the Examiner intended to refer to the foregoing step (3) (see col. 11, lines 16-20).

However, considering steps (3) to (5) (col. 11, lines 16-30) of the Westesen et al. reference, the Examiner still overlooks the fact that in step a) according to Applicant's Claim 16, active substance A) and dispersant B) are suspended in an aqueous phase. The Examiner contends that "it would be obvious to (…) melt the drug before or after it was suspended in

dispersant" (see also above).

Applicant's can not understand how the Examiner can conclude "dispersant" in his statement. Applicants respectfully point out, that in either case, the "drugs or other bioactive substances (…) may be melted together with the lipids (…) or may be dissolved, solubilzed or dispersed in the lipid melt" (see col. 11, lines 16-20), that "the dispersion medium is heated (..) before mixing" (see col. 11, lines 21-22) and that thereafter "the melted lipid compounds are emulsified in the dispersion medium" (see col. 11, lines 25-26).

Thus the Westesen et al. reference does not disclose suspending the active substance in an aqueous phase with the SLP production method according to col. 11 lines 6-57, but only its dissolution, solubilzation or dispersin in the lipid melt.

The Examiner further contends that the Westesen et al. reference discloses "the suspension of active agent with an aqueous solution is also disclosed", by citing that "stabilizers are added either to the lipid or bioactive agent or to the aqueous phase only, depending on their physicochemical characteristics".

First, Applicant's respectfully request that the Examiner confirms that the Examiner refers to the production method as disclosed in the abstract of the Westesen et al. reference. In the following Applicants will presume that the quoted phrase is based upon the abstract.

Applicants can not understand how the Examiner can conclude from the process as described in the abstract of the Westesen et al. reference, that a suspension of active agent with an aqueous solution is disclosed. Reading step (2) of the method disclosed in the abstract – which is in line with the cited passage of the Examiner – the Westesen et al. reference only discloses that "Stabilizers (..) (may be) added (…) to the aqueous phase."

Thus, the limitation of Applicants' invention according to Claim 16, 26 and 40, that an active substance A) which is solid at room temperature is suspended in an aqueous phase is still not met by the Westesen et al. reference.

Applicants have further added the limitation that step a) of the method according to

Claims 16. 26 and 40 is conducted at room temperature. It's apparent that accordingly the active substance, which is solid at room temperature, is suspended while still solid.

The amendment was done to obviate the argumentation of the Examiner that it's arbitrary to melt the solid active before or after adding compressible fluid, as no alteration of the end product would result.

Applicants have pointed out in response to previous office actions that the sequence is not arbitrary, as the exposure of the active to high temperatures shall be limited to the greatest possible extent, as such exposure to elevated temperatures, when melted results in at least partial disintegration of the active substance, which surely can be considered to be an alteration of the final product.

From the foregoing and from the fact that the Timothy et al. reference discloses neither an alteration of sequence nor a suspension of active substance with an aqueous phase and later heating of the mixture formed after addition of a compressible fluid to form an emulsion, but only addition of active to supercritical CO2 gas, it's apparent that the combination of the Westesen et al. reference and the Timothy et al. reference can not render Applicants Claims 16, 26 and 40 obvious.

From the foregoing, it is clear that Applicants' claims are not unpatentable over Westesen et al. (US 5,885,486) in view of Timothy et al. (Biotechnol. Prog. 2000, 16, 402-407) and the rejection of claims 16-36 and 40-45 under 35 U.S.C. 103(a) as obvious over Westesen et al. (US 5,885,486) in view of Timothy et al. (Biotechnol. Prog. 2000, 16, 402-407) should now be withdrawn.

Claim 42 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Westesen et al. (US 5,885,486) in view of Timothy et al. (Biotechnol. Prog. 2000, 16, 402-407) and further in view of Rochling et al. (US 6,602,823).

The Rochling et al. reference, as the Westesen et al. reference and the Timothy et al. reference, neither discloses suspending at least one active substance A) and at least one

dispersant B) in an aqueous phase, as outlined before, nor the sequence of steps as outlined in Applicants Claims 16, 26 and 40. Thus, and further due to the fact that Claim 42 incorporates all the limitations of Claims 16. 26 and 40, the Rochling et al. reference can not render Applicants Claim 42 obvious if read together with Westesen et al. in view of Timothy et al.

From the foregoing, it is clear that Applicants' claims are not unpatentable over Westesen et al. (US 5,885,486) in view of Timothy et al. (Biotechnol. Prog. 2000, 16, 402-407) and further in view of Rochling et al. (US 6,602,823) and the rejection of Claim 42 under 35 U.S.C. 103(a) as obvious over Westesen et al. (US 5,885,486) in view of Timothy et al. (Biotechnol. Prog. 2000, 16, 402-407) and further in view of Rochling et al. (US 6,602,823) should now be withdrawn.

In view of the present amendments and remarks it is believed that claims 16-36 and 40-45 are now in condition for allowance. Reconsideration of said claims by the Examiner is respectfully requested and the allowance thereof is courteously solicited.

CONDITIONAL PETITION FOR EXTENSION OF TIME

If any extension of time for this response is required, Applicant requests that this be considered a petition therefor. Please charge the required petition fee to Deposit Account No. 14-1263.

ADDITIONAL FEE

Please charge any insufficiency of fee or credit any excess to Deposit Account No. 14-1263.

Respectfully submitted,
NORRIS, McLAUGHLIN & MARCUS

By /William C. Gerstenzang/
William C. Gerstenzang
Reg. No. 27,552

WCG/dmm

875 Third Avenue- 18th Floor
New York, New York 10022
(212) 808-0700